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THE RICIN METHOD OF JACOBY-SOLMS FOR THE QUANTITATIVE ESTIMATION OF PEPSIN.

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THE various methods for the quantitative determination of pepsin in the gastric juice are numerous and ingenious, although but few have survived the test of time and corroboration. The older methods of Brücke, Grützner, Jaworski, Hammerschlag, and Oppler are of interest but of no practical value, while the Mette method has been and is still being so extensively assailed that its position, despite the advocacy of Pawow, seems to be uncertain. The above-named methods have been so frequently described that the omission of their review may be dispensed with.[1]

In 1906, Jacoby,[2] while engaged in a research on ricin, found that a solution of this substance in 1 per cent. sodium chloride solution became cloudy owing to the insoluble albuminous body contained in the substance, but that if pepsin were added to it the solution cleared up rapidly and completely. Jacoby hinted at the clinical application of this observation, but no attention was given the subject until Solms, working under Jacoby, published his paper the following year.

In this article he gives in clear detail the description of his method which he claims is easy, practicable, and inexpensive, and apparently does away with many of the difficulties surrounding the Mette test.

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[1] For bibliography see Farr and Goodman, Archives of Internal Medicine, 1908, i, 648.

[2] Arb. a. d. path. Institut. zu Berl., Feier, Johannes Orth, Berlin, 1906, p. 655.

The following description of Solms'[3] technique is copied from the paper of Farr and Goodman. The only materials needed are a solution of ricin and a $\frac{n}{10}$ hydrochloric acid solution.

"The ricin solution is made by dissolving 0.5 gram of ricin in 50 c.c. of 5 per cent. sodium chloride solution and filtering. (The ricin used by Solms was obtained from the Vereinigte chemische Werke, Charlottenburg, Salzufer 16, costing 2 marks for 10 grams. Solms preferred this preparation of ricin to Merck's, principally on account of the limited supply, and the great cost of the latter.) The filtered ricin solution has a somewhat cloudy appearance, but on the addition of 0.5 c.c. of $\frac{n}{10}$ hydrochloric acid becomes decidedly milky. The milky appearance is cleared up by pepsin.

"His technique is as follows: The gastric juice is obtained by extracting the stomach contents one hour after the ingestion of an Ewald-Boas test breakfast. He tests this for the presence of free hydrochloric acid, then determines the total acidity, and in appropriate cases examines for lactic acid. According to his findings he makes varying dilutions of the contents with distilled water. In cases of hyperacidity he dilutes the filtered contents from 1 to 100 to 1 to 10,000, whereas in cases of anacidity or subacidity the dilutions vary from 1 to 10 to 1 to 100. In normal cases he dilutes from 1 to 100 to 1 to 1000.

"In each of five test tubes he puts 2 c.c. of the filtered ricin solution; then with another graduated pipette he adds 0.5 c.c. $\frac{n}{10}$ hydrochloric acid, which causes the mixture to become very cloudy. Having numbered the test tubes, 1, 2, 3, 4, and 5, he puts in the first tube 1 c.c. of boiled gastric juice; in the second, 0.9 c.c.; in the third, 0.8 c.c.; in the fourth, 0.5 c.c.; and in the fifth, 0 c.c. Then he takes the unboiled juice and, having diluted 1 c.c. of juice with 99 c.c. of water, he puts in the first tube 0 c.c.; in the second, 0.1 c.c.; in the third, 0.2 c.c.; in the fourth, 0.5 c.c.; and in the fifth, 1 c.c., so that in each tube there are 3.5 c.c. of fluid. The test tubes are then corked and put in an incubator, where they are allowed to stand for three hours; at the end of this time they are taken out and the tubes examined to see with what dilution the ricin has been cleared up. If an incubator is not at hand, the tubes can be left at room temperature, of course, for a correspondingly longer time.

"In order to obtain a convenient expression of the pepsin contents of a gastric juice, he designates that amount of pepsin contained in 1 c.c. of a 1 to 100 dilution, which is capable of clearing up the ricin solution after three hours' standing in an incubator, as 100 pepsin units. This he has decided on as the normal standard, because after many examinations of specimens of normal acidity he found the ricin to be cleared up by 1 c.c. of a solution diluted 1 to 100."

Solms divided the specimens of gastric juice according to the acidity as follows: Normal, "almost normal," anacidity or subacidity, and hyperacidity. Under normal acidity are cases showing a positive reaction for free hydrochloric acid with Töpfer's test and Congo paper, and a total acidity of between 40 and 60. "Almost normal" are cases showing a total acidity between 30 and 40, and 60 and 70, with presence of free HCl. Below these values are cases of anacidity or subacidity, and cases showing a total acidity above 70 he calls hyperacidity.

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[3] Ztschr. f. klin. Med., 1907, lxiv, 159.

He reports 12 cases of normal acidity, seven of which showed 100, four, 200, and one, 500 pepsin units, and concludes that pepsin units between 100 and 200 may be considered as the normal. Six cases of "almost normal" gastric acidity (between 30 and 40) showed the same thing as did six cases between 60 and 70. In twenty cases of subacidity there was a marked diminution of pepsin units, generally between 10 and 20 units, in some cases below this, so that the amount of pepsin could not be estimated. Thirteen cases of hyperacidity showed a normal pepsin value and in but two cases was the amount of pepsin abnormally high, once 1000 units and in another instance 500 units.

Witte[4] has published a series of 50 patients on which the estimation of pepsin was made by means of ricin and believes the Jacoby-Solms method is exact and simple and is to be strongly recommended. He alters the technique very slightly, suggesting for normal cases a tube containing a dilution of 1 to 50, and in hypoacidity diluting the gastric juice 1 to 1, 1 to 10, 1 to 20, etc. He believes in this way he can detect mimimal amounts of pepsin. Witte has not followed the classification of Solms as to "almost normal" cases, but arranges his series in normal, sub- or anacidity, and hyperacidity. His conclusions are in the main the same as Solms' and he recommends the method very strongly. He queries, however, if there is not a grave source of error, inasmuch as there is no uniform acidity in the test tubes, and he thinks the optimum acidity is disturbed. He suggests for exact scientific work, a neutralization of the acid then by the addition of decinormal hydrochloric acid bringing the acidity to a uniformity. For clinical purposes, however, this not necessary.

Gross[5] objects to the ricin method on one point, and that is that the ricin used by Solms is very impure and there is no way of determining just how much albuminous substance is contained in it. This would seem to be a valid objection, but so far has not been fruitful of error as Solms, Witte, and I have obtained similar results, each working with separate specimens of ricin.

Solms is particularly insistent that studies with his method be carried out according to his description, in order that comparative studies may be obtained, which may be of value in diagnosis and therapeusis of gastric diseases. In our series of cases we have followed to the minutest detail Solms' directions, and while not varying from it have chosen in many cases to report the total acidity, free acid, combined acidity, and the acid salts. Control of Solms' method by means of the Mette test was made in ceratin cases by Dr. Farr and reported by us in connection with another phase of pepsin determination.[6] The arrangement of our tables differs slightly from that of Solms inasmuch as we do not favor "almost normal." This seems to be an injudicious subdivision, and we prefer to call gastric juice with total acidity between 40 and 60 normal, and below or above the subacidity or hyperacidity respectively.

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[4] Berl. klin. Woch., 1907, p. 1338.

[5] Ibid., 1908, p. 643.

TABLE I.—NORMAL ACIDITY (40–60).

Serial number.	Total acidity.	Free HCl.	Combined HCl.	Acid salts.	Rennin.	Ricin.	Mette.	Diagnosis.	Case number.
1	40	30	5	5	+	100–200	3.8 (14.4)	Hyperchlorhydria.	464
2	44	26	2	16	+	200	3.2 (10.2)	Gastro-enteroptosis.	505
3	45	20	20	5	+	100	Not made.	Gastric neurosis.	663
4	48	10	26	12	+	100	4.9 (24.0)	Chloro-anemia.	311
5	50	18	14	18	+	10	3.9 (15.2)	Chronic gastritis.	570
6	50	30	15	5	+	200	4.4 (19.4)	Migraine; dilatation of stomach.	511
7	54	34	18	12	+	100–200	4.3 (18.5)	Gastric neurosis.	434
8	54	36	8	10	+	100	Not made.	Tuberculous enteritis.	659
9	56	24	18	14	+	100	Not made.	Cholecystitis.	884
10	58	30	16	12	+	100 not clear	3.7 (13.7)	Hyperchlorhydria.	402
11	58	34	16	8	+	100	3.0 (9.0)	Neurasthenia; gastric neurosis.	449
12	60	45	5	10	+	100	5.2 (27.0)	Cholecystitis; hyperchlorhydria.	791

Normal acidity (40 to 60). In these cases we have found the pepsin unit to be between 100 and 200 and agree with Solms in regarding this as the normal. Using the Mette test as a control we have found a certain parallel between the two, both giving normal values, although the ricin method does not show the finer variation disclosed by the Mette method (Table I).

TABLE II—SUBNORMAL ACIDITY (BELOW 40).

Serial number.	Total acidity.	Free HCl.	Combined HCl.	Acid salts.	Rennin.	Ricin.	Mette.	Diagnosis.	Case number.
1	35	0	15	20	0	10–20	2.3 (5.3)	Endarteritis; chronic tuberculosis.	140
2	28	6	14	8	Slow.	10	2.8 (7.8)	Cholelithiasis; gastritis.	251
3	26	0	..	..	..	20–50	2.0 (4.0)	Polycythemia; chr. gastritis (vomitus).	814
4	26	8	6	12	Slow.	10–20	3.3 (10.9)	Gastric neurosis.	579
5	25	0	0	0	Very slow.	10	0.8 (0.64)	Pyelitis.	189
6	22	0	..	..	..	10	1.0 (1.0)	Lactic acid +; chronic gastro-enteritis.	813
7	22	0	0	0	+	0	3.4 (11.6)	Chronic gastritis.	571
8	20	0	0	0	0	0	0.1 (0.1)	Anacidity.	576

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[6] Loc. cit.

TABLE III—HYPERACIDITY (ABOVE 60).

Serial number.	Total acidity.	Free HCl.	Combined HCl.	Acid salts.	Rennin.	Ricin.	Mette.	Diagnosis.	Case number.
1	62	30	22	8	+	100-200	Not made.	Goitre; dilated stomach.	871
2	62	34	6	22	+	100	2.8 (7.8)	Psoriasis; eczema.	520
3	62	36	20	6	+	100-200	4.1 (16.8)	Gastric neurosis.	300
4	62	16	40	6	+	10	3.8 (14.4)	(Vomitus); carcinoma pylorus.	227
5	64	40	20	4	+	100	3.3 (10.9)	Neurosis.	575
6	64	30	24	10	+	100	Not made.	Nephritis; gastritis.	824
7	64	48	10	6	+	100	3.1 (9.6)	Adhesions; hyperchlorhydria.	615
8	65	40	5	20	+	100-200	3.6 (13.0)	Glycosuria.	500
9	65	40	15	10	+	100	3.4 (11.6)	Syphilis; neurasthenia.	176
10	66	40	11	15	+	100	2.8 (7.8)	Myalgia.	680
11	66	36	22	8	+	100	3.2 (10.2)	Tachycardia.	236
12	66	40	20	6	+	100	Not made.	Gastroptosis; gastric neurosis.	225
13	68	24	29	15	+	200	3.6 (13.0)	Frontal sinusitis; neurosis; hyperchlorhydria.	423
14	68	42	20	6	+	200	4.3 (18.5)	Gout; neurosis; alcoholic gastritis.	498
15	68	34	26	8	+	100 not clear.	3.3 (10.9)	Pancreatitis; hyperchlorhydria.	356
16	68	46	16	6	+	100-200	4.6 (21.2)	Cholecystitis; gastric ulcer.	322
17	68	44	6	18	+	100-200	5.9 (34.8)	Chronic appendicitis; gastric neurosis.	757
18	70	40	25	5	+	100	Not made.	Jaundice; cholecystitis.	664
19	70	40	15	15	+	100-200	4.0 (16.0)	Gastritis; hyperchlorhydria.	734
20	70	54	15	1	+	1000	5.8 (33.6)	Hour-glass contraction of stomach; pyloric adhesions.	282
21	70	46	12	12	+	100	3.2 (10.2)	Fibroid of uterus; hyperchlorhydria.	371
22	74	44	22	8	+	100	4.7 (22.0)	Hyperchlorhydria; pylorospasm; cholecystitis; chronic appendicitis.	335
23	75	55	15	5	+	100	3.0 (9.0)	Hyperchlorhydria.	538
24	75	40	10	25	+	100-200	3.0 (9.0)	Exophthalmic goitre.	455
25	76	30	32	14	+	100	4.0 (16.0)	Appendicitis.	326
26	78	56	20	2	+	100	3.5 (12.3)	Chronic appendicitis.	593
27	78	64	2	12	+	1000	3.8 (14.4)	Appendicitis; hyperchlorhydria.	476
28	78	36	26	16	+	100	3.9 (15.2)	Hyperchlorhydria.	450
29	78	40	16	22	+	100	3.8 (14.4)	Gastric ulcer.	430
30	80	55	15	10	+	100	3.4 (11.6)	Hyperchlorhydria.	678
31	80	55	20	5	+	100	3.0 (9.0)	Hyperchlorhydria.	585
32	82	52	18	12	+	100	3.0 (9.0)	Hyperchlorhydria.	T.T.M.
33	82	52	14	16	+	100	3.8 (14.4)	Bronchitis; gastritis.	599
34	82	54	24	4	+	100	3.4 (11.6)	Gastritis.	689
35	84	52	28	4	+	100	3.1 (9.6)	Hyperchlorhydria.	T.M.B.
36	84	60	20	4	+	100	Not made.	Neurosis; hyperchlorhydria.	883
37	85	35	35	15	+	100	2.9 (8.4)	Neurasthenia; gastroptosis.	692
38	85	55	25	5	+	100	2.6 (6.8)	Gastric neurosis.	667
39	86	48	28	10	+	100	4.9 (24.0)	Gastric neurosis.	561
40	86	58	2	26	+	100	5.2 (27.0)	Appendicitis: hyperchlorhydria.	273
41	88	54	22	12	+	500	2.8 (7.8)	Cholecystitis; hyperchlorhydria.	171
42	88	58	24	6	+	100-200	4.9 (24.0)	Frontal and ethmoidal sinusitis; hyperacidity.	785
43	88	62	12	14	+	1000	5.3 (28.0)	Gastritis; hyperchlorhydria.	334
44	95	60	25	10	+	500	3.1 (9.6)	Neurosis; hyperchlorhydria.	489
45	100	45	20	35	+	100	2.9 (8.4)	Gastric ulcer.	597
46	106	94	10	2	+	100-200	Not made.	Cystitis; enteritis.	828
47	110	62	32	16	+	200	3.7 (13.7)	Epilepsy (?).	713

Subnormal acidity, below 40. Here again we agree with Solms, as there was a marked reduction of pepsin units co-relative with diminished acidity. The Mette method also gave low pepsin value with the exception of two cases, Nos. 4 and 7, in which the amount was normal. This discrepancy between the two methods is more apparent than real, however, as the control tests used for the Mette estimations were also high (Table II).

Hyperacidity above 60. In 5 cases Nos. 20, 27, 41, 43, and 44 the pepsin value was high. That this sometimes occurs has been pointed out by Solms, but in the majority of cases our results showed normal pepsin units. The Mette test in Cases 20 and 43 was also high, whereas in Case 27 it showed a normal value. In Cases 41 and 44 the Mette was low, which is explained by the low result obtained in the control experiment (Table III).

We have thus been able to study the estimation of pepsin by the Jacoby-Solms method in a large series of cases, and we can corroborate Solms' findings. The method is extremely simple, cheap, and sufficiently accurate for all clinical purposes. The rapidity with which one obtains a result is not the least important factor in advocating its use by clinicians. That it does not possess the finer variations of the Mette method cannot be denied, but in the present state of our knowledge of pepsin this cannot be offered as an objection, as this so-called advantage has been of no help to us in diagnosis.

Experiments were made in a limited number of cases to determine if a uniform acidity made any difference in the final result, and whether the law of Schültz held good for the ricin method. So far both of these questions must be answered negatively.

Conclusions: (1) The normal pepsin unit as disclosed by the ricin method is between 100 and 200. (2) Cases of hyperacidity with few exceptions are not accompanied by a corresponding increase of pepsin. (3) Cases of subacidity are invariably associated with a diminution of pepsin. (4) The ricin method is to be recommended on account of its simplicity, cheapness, accuracy, and rapidity.